AF/1652

PATENT
Customer No. 22,852
Attorney Docket No. 09526.0001-01000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Jacques FASTREZ et al.	)	Group Art Unit: 1652
	)	
Application No.: 08/978,607	)	Examiner: T. Saidha
	)	
Filed: November 11, 1997	)	
	)	
For: CHIMERIC TARGET MOLECULES HAVING A REGULATABLE ACTIVITY	)	Confirmation No.: 4607

Attention: Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SUBSTITUTE APPEAL BRIEF UNDER BOARD RULE § 41.37

In support of the Notice of Appeal filed September 30, 2003, and further to Board Rule 41.37, Appellant presents this brief and enclose herewith a check for the fee of $500.00 required under 37 C.F.R. § 1.17(c).

In view of the Decision on Petition to Withdraw the Holding of Abandonment dated July 15, 2004, and the Petition for an Extension of Time for five months and fee filed February 7, 2005, this Appeal Brief is due by February 15, 2005, and is timely filed.

This Appeal responds to the April 1, 2003, Office Action and the July 30, 2003, Advisory Action finally rejecting claims 13-29.

If any additional fees are required or if the enclosed payment is insufficient, Appellants request that the required fees be charged to Deposit Account No. 06-0916.

Table of Contents

Real Party In Interest

The assignee, BioVeris Corporation, 16020 Industrial Drive, Gaithersburg, MD 20877, is the real party in interest.

Related Appeals and Interferences

There are currently no other appeals or interferences, of which Appellants, Appellants' legal representative, or Assignee are aware, that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

Status Of Claims

The application was filed as U.S. Application No. 08/978,607 on November 11, 1997, as a continuation in part application of US Application No. 08/757,425 filed on November 27, 1996, now abandoned. The subject application was filed with claims 1-22. In response to a Restriction Requirement mailed July 7, 1998, claims 13-22 were elected for prosecution.

Claims 23-29 were added by an amendment filed April 2, 2002. Claims 30-38 were added by an amendment filed January 14, 2003. Finally, claims 30, 34, 37, and 38 were amended and claim 36 was cancelled by the Amendment After Final filed on July 8, 2003, which was entered by the Examiner.

Claims 13-29 of this application were finally rejected in an Office Action mailed December 27, 2002 and claims 30-35 and 37-38 were indicated as allowable in the Advisory Action mailed on July 30, 2003.

The status of the claims is as follows:

Allowed claims: 30-35 and 37-38

Claims objected to: None

Claims rejected: 13-29.

Claims cancelled: 1-12 and 36.

The claims as amended on February 7, 2005, and on March 31, 2005, are set out in the Appendix, attached hereto.

The claims on appeal are 13-29.

Status Of Amendments

The Amendment After Final filed July 8, 2003, was acknowledged and entered. The amendment brought claims 30-35 and 37-38 in condition for allowance. A Second Amendment After Final was filed on February 7, 2005, and a Supplemental Amendment After Final was filed March 31, 2005. During a telephonic interview on March 30, 2005, with Applicants undersigned representative, the Examiner indicate that the Amendment filed February 7, 2005, would be entered and that, if Applicants' Petition Under 37 C.F.R. §1.183 To Waive the Requirements of 37 C.F.R. §41.33(b) is granted, the Supplemental Amendment filed March 31, 2005, would also be entered.

Summary Of Claimed Subject Matter

The claims on appeal recite methods for detecting an analyte in a sample using a chimeric enzyme, the activity of which is altered in the presence of the analyte. *See* Specification at 2, ll. 1-3. The chimeric enzymes of the invention comprise a starting enzyme and at least one mimotope[1] that is a binding site for a binding molecule. *See id.*, ll. 10-18. The starting enzyme is selected for a desired detectable activity. *See id.*, l. 23. The mimotope, which can be either inserted or engineered into the starting enzyme by a variety of genetic and chemical techniques, is selected for recognition of the desired binding molecule. *See id.* at 11, ll. 11-13. Binding of the binding molecule to the mimotope either increases or decreases an activity of the chimeric enzyme. *See id.* at 2, ll. 12-18.

In certain embodiments encompassed by independent claim 13, the analyte can reduce binding of the binding molecule to the mimotope, thereby decreasing the effect of the binding molecule on the activity of the chimeric enzyme. *See id.* at 2, ll. 5-7; at 4, ll. 12-18; at 17, ll. 13-15.

In certain embodiments encompassed by independent claims 13 and 20, the analyte itself can be the binding molecule and alter the activity of the chimeric enzyme. *See id.* at 16, ll. 14-21.

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[1] The "starting enzyme" is the molecule into which the mimotope is inserted to produce the chimeric enzyme. *See* Specification at 5, ll. 6-16. A "mimotope" is a sequence that is recognized by a binding molecule, but differs from the naturally occurring binding site by at least one amino acid. *See id.* at 10, ll. 13-19. The application discloses that one advantage of employing a mimotope is that one can design or screen for mimotopes for a specific binding molecule without any knowledge of the structure of its natural epitope. *See id.* at 4-16.

According to all of the claims on appeal, the presence and/or amount of the analyte in the sample can be determined by monitoring or detecting this change in activity of the chimeric enzyme.

Grounds of Rejection

A. Claims 13-29 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification;

B. Claims 13-29 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention;

C. Claims 13 and 20 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Benito et al., J. Biol. Chem. 271: 21251-21256 (1996); and

D. Claims 13 and 20 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Brennan et al., Protein Engineering 7: 509-514 (1994).

Argument

A. The Claims Are Enabled

The Examiner rejects claims 13-29 stand under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. *See* Advisory Action mailed July 30, 2003 ("Advisory Action"), at 2. According to the Examiner, "[t]he claims are directed to a method of determining the presence of an analyte using any (a) chimeric enzyme as the starting enzyme, wherein said chimeric enzyme is constructed by inserting a sequence of said mimotype (binding site moiety) into a sequence of said starting enzyme by replacing at least one amino acid of the starting enzyme with a sequence of said mimotype." *Id.* (emphasis original). The Examiner contends that "the guidance provided for a single site specific chimeric β-lactamase is inadequate for one skilled in the art to develop a method using any chimeric enzyme construct for determining the presence or amount of an analyte in a test sample." *Id.* at 2-3.[2]

Appellants respectfully traverse. The Examiner is actually rejecting claims 13-29 as allegedly not being enabled because he contends that undue experimentation would be required in order to make the entire scope of chimeric enzymes that might be used in the claimed methods. But the law requires only that Appellants enable the claimed invention, not other inventions that might be useful in practicing the claimed invention. *See* M.P.E.P. § 2164; *see also Phillips Petroleum Co. v. U.S. Steel Corp.*, 673 F. Supp. 1278, 6 U.S.P.Q.2d 1065 (D. Del. 1987), aff'd, 865 F.2d 1247, 9 U.S.P.Q.2d 1461 (Fed. Cir. 1989). Here, the claimed invention is an assay method and that method is

[2] The Examiner fails to explain why he believes that claim 24, which recites that the starting enzyme is β-lactamase, is not enabled.

fully enabled by the specification. The claims do not encompass chimeric enzymes, which, if novel in a particular case, would be separately patentable.

The methods of claims 13 and 20 require forming a mixture comprising: (1) a chimeric enzyme comprising the activity of which is modulated upon binding of a binding molecule to a mimotope in the enzyme, (2) a test sample, and (3) a substrate upon which the chimeric enzyme catalytically acts. Claim 13 requires an additional component: a binding molecule that binds to the mimotope and thereby modulates the activity of the enzyme. In claims 13 and 20, the presence or amount of the analyte in the test sample is determined by measuring the amount of substrate catalysis.

One skilled in the art, guided by the specification, could use the claimed methods without undue experimentation to perform the full scope assays encompassed by the claims. The specification provides both general guidance and specific examples for all necessary steps. Figures 4 and 5 show the entire assay method. In these figures, a measurable signal (in this case, enzyme activity [Kcat]), is shown as a function of analyte concentration (in this case, PSA antibody concentration), thereby measuring the presence or amount of the analyte. Example 3 describes another specific example, where the analyte of interest was biotin. Thus, in contrast to the Examiner's assertion that ". . . such a binding function for determining the presence or amount of an analyte in a test sample is neither exemplified nor a matter of routine experimentation. (Page 4, line 5)," the specification provides three specific examples. One skilled in the art would readily appreciate that the assay for PSA antibodies could easily be converted into an assay for PSA itself, which would block antibody binding to the chimeric enzyme.

Although the Examiner contends that the only guidance provided is "a single site specific chimeric β-lactamase," the specification in fact describes the preparation of 5 libraries of recombinant bacteriophage expressing β-lactamase chimeras. *See* Example 1. Two of these libraries, lib1A-B and lib1D, contain phage comprising random six amino mimotopes inserted in place of β-lactamase residues E104/Y105 and V103/Y105, respectively. *See* Specification at 21, ll. 3-5; Tables 1-3. A third library, lib3d, contains 80,000 different clones comprising random five amino mimotopes inserted in place of β-lactamase residues T271/M272. *See* Specification at 22, ll. 9-12. The fourth library, lib3f, contains about 4,000,000 different clones comprising random six amino mimotopes inserted in place of β-lactamase residue T271. *See id.* at 22, l. 18, to 23, l. 10. Lastly, the fifth library, lib rec4b, contains approximately 50,000,000 different clones expressing chimeric enzymes useful in the claimed assay methods. *See id.* at 24, ll. 16-19.

The specification also discloses methods for isolating from libraries of such recombinant bacteriophage chimeric enzymes useful in an assay according to the invention for a specific analyte. *See* Examples 2 and 3. These methods are exemplified using two commercially available antibodies to prostate specific antigen, psa10 and psa66, to identify chimeric enzymes that could be used in an assay for that antigen according to the invention. It would have been readily apparent to one skilled in the art at the time the invention was made that the same methods could be used to identify chimeric enzymes for detecting other analytes of interest simply by changing the antibody or binding protein used in the isolation procedure.

Here, Appellants have enabled one skilled in the art to make and use the full scope of that which they claim: a method for determining the presence or amount of an analyte in a test sample. There is no requirement that Appellants also enable the skilled artisan to use all possible starting enzymes to prepare chimeric enzymes that for reasons unrelated to the invention one might wish to use in the claimed methods. Even in this regard, however, the Examiner's analysis, which is based on the factors from *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988), is flawed.

The Examiner acknowledges that the factors to be considered in determining whether undue experimentation is required are (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working examples, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. *See* Advisory Action at 3; Office Action mailed April 1, 2003 ("Office Action") at 2-3. The Examiner considers only three of these factors that he considers "most relevant to this rejection": the quantity of experimentation necessary, the amount of direction or guidance presented, and the predictability or unpredictability of the art. Advisory Action at 3; Office Action at 3.

Wands, however, describes a balancing test, and it is impermissible to consider only those test factors that support the Examiner's position. *See* M.P.E.P. § 2164.01(a) ("The examiner's analysis must consider all the evidence related to each of [the *Wands*] factors, and any conclusion of nonenablement must be based on the evidence as a whole"). Here the factors the Examiner ignores support the conclusion that claims 13-29 are enabled.

c. The Presence or Absence of Working Examples. The specification describes the construction of 5 libraries of recombinant bacteriophage expressing β-lactamase chimeras with mimotopes inserted at several sites. *See* Example 1. The specification also provides 2 examples of screening recombinant libraries for mimotopes that bind various antibodies, thereby regulating enzyme activity. *See* Example 2. Finally, the specification provides an example of screening recombinant libraries for mimotopes that bind other molecules, e.g., streptavidin, that regulate enzyme activity. *See* Example 3.

d. The Nature of the Invention. The invention is an assay that requires a chimeric enzyme, over 50,000,000 of which have been prepared by methods described in Example 1, (2) a test sample, which could be provided by, for example, the user, and (3) a substrate upon which the chimeric enzyme catalytically acts, many examples of which are known in the art, for example, penicillins and cephalosporins.

e. The State of the Prior Art. The Examiner has identified two references published before Appellants' filing date that describe chimeric enzymes comprising epitopes rather than the mimotopes of the claimed assay methods. Benito et al., J. Biol. Chem. 271: 21251-21256 (1996) describe a chimeric enzyme having the main antigenic region of foot-and-mouth disease virus serotype C_1 inserted into β-galactosidase. *See* Benito et al., Abstract ("The main antigenic region of foot-and-mouth disease virus serotype C, also called site A, has been inserted in zones of the β-

galactosidase important for stabilization of the active site . . .”). Antibody binding to the viral epitope modulates β-galactosidase activity. *See id.* (“In these constructs, the binding of the specific antibodies directed to the foreign peptide causes an increase of the β-galactosidase activity up to about 200%”). Brennan et al., Protein Engineering 7: 509-514 (1994), describe a chimeric enzyme having an epitope from the HIV-1 protein V3 loop inserted into bacterial alkaline phosphatase. *See* Brennan et al., Abstract, page 509. Again, antibody binding to the viral epitope modulates enzyme activity. Brennan et al., page 509. There could be no credible dispute that one skilled in the art would be forced to undertake undue experimentation in order to substitute a mimotope for the epitopes of Benito and Brennan.

f. The Relative Skill of Those in the Art. One skilled in the art would likely have a Ph.D or other advanced degree.

h. The Breadth of the Claim. The claims encompass assays for a large number of analytes of interest. However, one skilled in the art does not have to prepare chimeric enzymes beyond those disclosed in the examples to practice the full scope of the claimed assays.

Moreover, when one applies the three *Wands* factors the Examiner did consider to the *claimed* invention, assay methods, they too support the conclusion that claims 13-29 are enabled.

a. The Quantity of Experimentation Necessary. The specification teaches one skilled in the art how to make libraries of recombinant bacteriophage

expressing β-lactamase-mimotope chimeras. *See* Example 1. The libraries contain more than 50,000,000 different chimeras. *See id.* The specification further teaches simple methods for screening the libraries to identify chimeras useful in essentially any assay within the scope of the claims. *See* Examples 2-3. Practicing the claimed assay methods requires no experimentation. One skilled in the art need only follow the guidelines provided by Appellants.

b. The Amount of Direction or Guidance Presented. As noted in (a), the specification provides explicit instructions for preparing and identifying chimeric enzymes useful for practicing the full scope of claims 13-29. Moreover, should the skilled artisan want to use an enzyme other than β-lactamase in the claimed methods, the specification provides the needed guidance. The specification directs the skilled artisan to start with an enzyme for which a selection assay can be designed, e.g., enzymes conferring drug resistance or antibiotic resistance or enzymes whose substrate and product differ by color or fluorescence. *See, e.g.*, Specification, page 18. The specification identifies 11 exemplary starting enzymes that have been displayed on phage and are directly amenable to selection for a desired activity. *See id.*, pages 2-3. The specification identifies three factors to consider when modifying a starting enzyme so that the activity depends on the presence or absence of a binding molecule. First, the specification teaches that modifications should be made near, but not in, the active site of the enzyme in order to increase

the likelihood that the chimeric enzyme will be active. *See id.,* pages 11-12. Second, the specification teaches that modifying regions that are not conserved between similar enzymes increases the likelihood that the activity of the chimeric enzyme will be maintained. *See id.,* sentence bridging pages 36-37. Third, the specification teaches that modifications that are expected to be on the outside surface of the enzyme increases the likelihood that the mimotope is accessible to the binding molecule. *See id.,* page 11. Tools for evaluating all three factors were well known to those skilled in the art at the time the application was filed, for example, the active site of an enzyme could be identified using LIGPLOT (Wallace A. C. et al., Prot. Eng., 8, 127-134, 1995); non-conserved regions in related enzymes could identified with the BlastP program, which is readily available at, for example, http://www.ncbi.nlm.nih.gov/BLAST/; over 5,000 3D protein structures were available at the time through the protein data bank (http://www.rcsb.org/pdb/holdings.html).

g. The Predictability or Unpredictability of the Art. There is no dispute that the art of developing assay methods using antibodies or other binding molecules is predictable.

All of the *Wands* factors clearly support the conclusion that the claimed invention is fully enabled by the specification. The rejection of claims 13-29 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification is incorrect and should be withdrawn.

B. The Claims Are Supported by the Specification

The Examiner also rejects claims 13-29 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. *See, e.g.*, Advisory Action at 9. According to the Examiner, "[c]laims 13-29 are directed to a method of determining the amount of analyte using any chimeric enzyme or 'the claimed genus' from any organism wherein any of the amino acid residues along the peptide chain is modified to make [a] chimeric enzyme." *Id.*, Office Action at 8. The Examiner also asserts that a representative number of β-lactamase species are not described in the application as-filed. *See* Advisory Action at 9-10; Office Action at 9-10.

Again however, the claimed invention is neither chimeric enzymes generally nor chimeric enzymes derived from β-lactamase. There is no "claimed genus" of chimeric enzymes. Rather, the claims recite methods of detecting an analyte in a sample, and it is this invention that must find support in the specification.

To support his position, the Examiner cites the specification at page 2, lines 10-12 for the proposition that "Applicants further argue that the invention is to a 'desired target (TM) which can be modified to have at least one binding site moiety (BSM) to which a binding molecule [can] attach.'" As an initial matter, the cited portion of the specification does not state that the invention "is to 'a desired target molecule.'" Rather, the specification states that "[I]n accordance with the present invention, a desired target

molecule (TM) can be modified . . .." Moreover, even if the Examiner's assertion were correct, this is not the invention claimed.[3]

The Examiner's position is akin to asserting that hypothetical claims to a novel immunoassay method would not be adequately supported unless the accompanying specification describes a representative number of antibodies that could be used in the assay. This is not the law. All that is necessary to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, is that the specification convey to one skilled in the art that the applicants were in possession of the *claimed* invention at the time of filing. *See Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997).

Appellants' "claimed invention" is an assay method. As described above, the specification presents three specific examples of the claimed assays: two for PSA antibodies and one for biotin. *See* Examples 2-3. Because the percent inhibition of the chimeric enzyme activity depends on the amount of anti-PSA antibody bound, one skilled in the art would immediately understand that the chimeric enzymes could be used in an assay to detect an analyte, prostate specific antigen, that would block antibody binding. The specification also describes libraries of recombinant bacteriophage from which chimeric enzymes useful in practicing the claimed assay methods for other analytes can be harvested. *See* Example 1. No one could seriously doubt that Appellants were in possession of the entire scope of the claimed assays

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[3] The Examiner also notes that, despite Applicants "argument," he could not find 10 exemplary target molecules on pages 2-3 of the specification. In fact, the cited portion of the specification lists 11 target molecules: β-lactamase, plasmin, prostate specific antigen, subtilisin, trypsin, alkaline phosphatase, β-galactosidase, staphylococcal nuclease, glutathione transferase, lysozyme, and catalytic antibodies.

simply by isolating from the existing recombinant libraries a chimeric enzyme using antibodies to other analytes.

The rejection of claims 13-29 under 35 U.S.C. § 112, first paragraph, as allegedly not being supported by the specification is incorrect and should be withdrawn.

C. Claims 13 and 20 Are Not Anticipated by Benito

Claims 13 and 20 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Benito et al., J. Biol. Chem. 271: 21251-21256 (1996). According to the Examiner, Benito et al. "teach a method for modulation of enzyme activity (β-Galactosidase) after insertion of an antigenic region of peptide (epitope or mimotope or binding site-moiety [sic]) into β-Galactosidase, which is mediated by antibody binding and further point to use of this hybrid or chimeric construct for the rapid detection of specific antibodies in a quick and simple homogeneous assay based on the calorimetric [sic] determination of β-Galactosidase activity." Advisory Action at 11; Office Action at 11. The Examiner concludes that Benito et al. teach all of the limitations of claims 13 and 20, thereby anticipating those claims. *See* Advisory Action at 12; Office Action at 11.

The Examiner is wrong. To anticipate a claim a reference must contain all of the elements of the claim. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986); *In re Marshall*, 578 F.2d 301 (C.C.P.A. 1978). Despite the Examiner's characterization of Benito et al., that reference describes nothing more than the incorporation of a linear viral ***epitope*** (i.e., the main antigenic region of foot-and-mouth disease virus serotype C_1) into β-galactosidase. Benito et al explicitly state that "[t]he recombinant VP1 peptide contains multiple overlapping

epitopes" and "protein M278VP1 is clearly activated by mAbs that recognize different B cell ***epitopes*** in the viral segment" Benito et al. at pages 21254-5 (emphasis added)).

In other words, contrary to the Examiner's assertion, the antigenic peptide of Benito et al. is an epitope and not a mimotope as claimed in claims 13 and 20. Appellants' specification could hardly be more clear that an epitope and a mimotope are not the same thing. *See, e.g.*, Specification at 10, ll. 13-14 ("A 'mimotope' is a determinant which is recognized by the same binding molecule as a particular 'epitope' but which has a different composition from the 'epitope.'"). Moreover, the specification discloses that using a mimotope is advantageous. *See id.* at 11, ll. 4-5 ("An advantage of employing a mimotope is that no knowledge of the structure of the epitope is required").

At least because Benito et al. do not describe a chimeric enzyme comprising a mimotope, that reference cannot anticipate claims 13 and 20. The rejection of claims 13 and 20 under 35 U.S.C. § 102(a) is improper and should be withdrawn.

D. Claims 13 and 20 Are Not Anticipated by Brennan

Claims 13 and 20 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Brennan et al., Protein Engineering 7: 509-514 (1994). According to the Examiner, "Brennan et al teach an epitope (mimotope) of an HIV protein inserted into bacterial alkaline phosphatase in creating a chimeric enzyme having a mimotope or epitope or binding site-moiety." Advisory Action at 12; Office Action at 11. This is the same error the Examiner makes in rejecting claims 13 and 20 as allegedly anticipated by Benito et al.

As with Benito et al., Brennan et al. clearly teach incorporation of a linear viral ***epitope*** (i.e., an epitope from the HIV-1 protein V3 loop), not a mimotope, into bacterial alkaline phosphatase. *See* Brennan et al., Abstract, page 509 ("An ***epitope*** from the HIV-1 gp120 protein V3 loop has been inserted...") (emphasis added). Even the title of the Brennan et al. reference is "Modulation of the enzyme activity by antibody binding to an alkaline phosphotase – ***epitope*** hybrid binding protein." Brennan et al., page 509 (emphasis added).

Once again, because Brennan et al., like Benito et al., do not teach or suggest incorporation of mimotopes into a starting enzyme, that reference cannot anticipate claims 13 and 20. The rejection of claims 13 and 20 under 35 U.S.C. § 102(b) is improper and should be withdrawn.

Conclusion

For the reasons given above, pending claims 13-29 are allowable and reversal of the Examiner's rejection is respectfully requested.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Appeal Brief, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 which are not enclosed herewith,

including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: March 31, 2005

By: 

William L. Strauss
Reg. No. 47,114

Claims Appendix to Appeal Brief Under Rule 41.37(c)(1)(viii)

13. A method for determining the presence or amount of an analyte in a test sample, comprising:

forming a mixture of (I) a chimeric enzyme comprising a starting enzyme and a mimotope, said mimotope including at least one amino acid, said chimeric enzyme having a sequence of said mimotope inserted in said enzyme or replacing at least one amino acid of said enzyme with the proviso that the activity of the chimeric enzyme is modulated upon binding of a binding molecule to the mimotope, (2) a test sample, (3) a binding molecule which binds to a mimotope of the chimeric enzyme and modulates the activity of the enzyme, and (4) a substrate upon which the chimeric enzyme catalytically acts; and

detecting the amount of catalysis of the substrate and thereby determining the presence or absence of said analyte of interest.

14. The method of claim 13, wherein the analyte competes with the chimeric enzyme for binding to the binding molecule.

15. The method of claim 13, wherein the analyte is prostate-specific antigen.

16. The method of claim 13, wherein the test sample is serum.

17. The method of claim 13, wherein the test sample contains the analyte.

18. The method of claim 13, wherein the binding molecule is said analyte.

19. The method of claim 13, wherein the binding molecule is an antibody.

20. A method for determining the presence or amount of an analyte in a test sample, comprising:

forming a mixture of (I) a chimeric enzyme comprising a starting enzyme and a mimotope, said mimotope including at least one amino acid, wherein said chimeric enzyme having a sequence of said mimotope inserted in said enzyme or replacing at least one amino acid of said enzyme with the proviso that the activity of the chimeric enzyme is modulated upon binding of a binding molecule to the mimotope, (2) test sample, and (3) a substrate upon which the chimeric enzyme catalytically acts; and

detecting the amount of catalysis of the substrate and thereby determining the presence or absence of said analyte of interest.

21. The method of claim 20, wherein the analyte and substrate contact the enzyme simultaneously.

22. The method of claim 20, wherein the analyte is contacted with the chimeric enzyme prior to contacting with the test sample and the substrate.

23. The method of claim 20, wherein the analyte is an antibody.

24. The method of claim 20, wherein the starting enzyme is β-lactamase.

25. The method of claim 20, wherein the test sample contains the analyte.

26. The method of claim 13, wherein the mimotope comprises any one of a sequence identified from SEQ *ID* NOs. 1-78.

27. The method of claim 20, wherein the mimotope comprises any one of a sequence identified from SEQ *ID* NOs. 1-78.

28. The method of claim 13, wherein the enzymatic activity of the chimeric enzyme in the unbound state is equivalent to that of the starting enzyme.

29. The method of claim 20, wherein the enzymatic activity of the chimeric enzyme in the unbound state is equivalent to that of the starting enzyme.

30. A method for determining the presence or amount of an analyte in a test sample, comprising:

forming a mixture of (I) a chimeric enzyme comprising β-lactamase and a binding site moiety, said binding site moiety including at least one amino acid, said chimeric enzyme having a sequence of said binding site moiety inserted in said enzyme or replacing at least one amino acid of said enzyme with the proviso that the activity of the chimeric enzyme is modulated upon binding of a binding molecule to the binding site moiety, (2) a test sample, (3) a binding molecule which binds to a binding site moiety of the chimeric enzyme and modulates the activity of the enzyme, and (4) a substrate upon which the chimeric enzyme catalytically acts; and

detecting the amount of catalysis of the substrate and thereby determining the presence or absence of said analyte of interest,

31. The method of claim 30, wherein the analyte competes with the chimeric enzyme for binding to the binding molecule.

32. The method of claim 30, wherein the binding molecule is said analyte.

33. The method of claim 30, wherein the binding molecule is an antibody.

34. The method for determining the presence or amount of an analyte in a test sample, comprising:

forming a mixture of (I) a chimeric enzyme comprising β-lactamase and a binding site moiety, said binding site moiety including at least one amino acid, wherein said chimeric enzyme having a sequence of said binding site moiety inserted in said enzyme or replacing at least one amino acid of said enzyme with the proviso that the activity of the chimeric enzyme is modulated upon binding of a binding molecule to the binding site

moiety, (2) test sample, and (3) a substrate upon which the chimeric enzyme catalytically acts; and

detecting the amount of catalysis of the substrate and thereby determining the presence or absence of said analyte of interest.

35. The method of claim 34, wherein the analyte is an antibody.

37. The method of claim 30, wherein the enzymatic activity of the chimeric enzyme in the unbound state is equivalent to that of the β-lactamase.

38. The method of claim 34, wherein the enzymatic activity of the chimeric enzyme in the unbound state is equivalent to that of the β-lactamase.

Evidence Appendix to Appeal Brief Under Rule 41.37(c)(1)(ix)

Appellants rely on no evidence in this appeal.

Related Proceedings Appendix to Appeal Brief Under Rule 41.37(c)(1)(x)

Appellants cite no related proceeding decisions in this appeal.